

### REMARKS

This responds to the Office Action mailed on October 4, 2007.

Claims 1-21, 24-44, 47-60 and 61 are pending in this application. However, the Examiner has withdrawn claims 47-57 as a result of the Restriction Requirement. Accordingly, claims 1-21, 24-44, 58-60 and 61 are under examination.

Claims 1, 4, 17, 18, 24, 27, 40, 41, 59 and 61 are amended.

In particular, the phrase “and wherein the mammal is a secretory leukocyte protease inhibitor (SLPI) deficient mammal” has been added to claims 1 and 24. Support for subject matter relating to treatment of SLPI-deficient mammals with wounds can be found throughout the specification as filed, for example, at page 2, lines 26-27; page 20, lines 28-29; page 22, lines 8-15 and in the Examples (see, especially, Example 6).

In addition, the term “an” has been deleted from claims 4 and 27, and the term “claims” has been amended “claim” in claims 17, 18, 40 and 41. Inadvertent errors in the dependencies of claims 18, 41, 59 and 61 have also been corrected.

Applicant submits that no new matter has been added to the application.

#### ***§112, First Paragraph, Rejection of the Claims***

Claims 1-21, 24-44 and 58-61 were rejected under 35 U.S.C. § 112, first paragraph, as allegedly lacking enablement. The Examiner acknowledges that the specification enables a method for promoting epithelial proliferation without eliciting production of IL-8, a method of blocking TNF-induced neutrophil activation by PEPI, and a method of forming a complex between PEPI and SLPI. However, the Examiner alleges that the specification lacks enablement for a method of wound healing or inhibiting inflammation in wild type mammals, by administering PEPI with or without SLPI (citing the specification at page 54, lines 12-17).

Claims 1 and 24 are now directed to treating wounds and inflammation in SLPI-deficient mammals by administering an effective amount of a composition comprising proepithelin (PEPI) to the mammals.

Applicant submits that there can be no doubt that SLPI-deficient mammals exhibit poor wound healing and that PEPI administration is an effective wound treatment for such SLPI-deficient mammals. For example, several references published since the filing date of the

application confirm that SLPI-deficient animals exhibit poor wound healing. See, Thuraisingam et al., *J. Invest. Dermatol.* 126: 890-901 (2006); Angelov et al., *Thromb. Haemost.* 92: 288-97 (2004); and Brunner, *Thromb. Haemost.* 92: 232-233 (2004) (submitted herewith in a Supplemental Information Disclosure Statement). Applicant's own data demonstrate that PEPI is useful for treating wounds in such SLPI-deficient mammals. In particular, Example 6 of Applicant's specification demonstrates that additional PEPI restores normal wound in SLPI-deficient animals. Therefore, there can be no doubt that administration of PEPI is beneficial for wound-healing in SLPI-deficient mammals.

Data also exists showing that humans with SLPI-deficiencies exhibit poor wound healing. In particular, SLPI expression is lower in elderly humans. See, Shugars et al., *Gerontology* 47: 246-253 (2001). Shugars et al. also discloses the following at page 247:

Recent studies have identified novel inhibitory activities for SLPI against commensal fungi (e.g., *C. albicans*), bacteria (e.g., *Escherichia coli* and *Staphylococcus aureus*), and viruses (e.g., HIV and influenza virus) as well as a role in *cutaneous wound healing*. (Emphasis added; citations omitted).

Further data exist showing that SLPI levels are lower in the cervicovaginal tissues and secretions of post-menopausal women, especially those with vaginal complaints such as genital itching, dryness or pain of the genital tract. See, Shimoya et al., *Maturitas* 54: 141-148 (2006). In addition, data available in the Gene Expression Omnibus (GEO) database of the National Center for Biotechnology Information (NCBI) shows that diabetic patients who have nephropathy due to an impaired tissue repair capability have lower levels of SLPI. See, [http://www.ncbi.nlm.nih.gov/projects/geo/gds/profileGraph.cgi?&dataset=pzZUA8&dataset=mpeaPh\\$&gmin=184.000000&gmax=1677.900000&absc=15967p1p1p1&gds=961&idref=32275\\_at&annot=SLPI](http://www.ncbi.nlm.nih.gov/projects/geo/gds/profileGraph.cgi?&dataset=pzZUA8&dataset=mpeaPh$&gmin=184.000000&gmax=1677.900000&absc=15967p1p1p1&gds=961&idref=32275_at&annot=SLPI). In particular, as described by the NCBI GEO disclosure, diabetic patients GSM15968 and GSM15969 exhibit lower levels of SLPI than non-diabetic controls (GSM15965, GSM15966 and GSM15967). The table shown below illustrates the differences in SLPI expression levels of these patients.

Sample	Value	Sample	Value
GSM15965	1409	GSM15968	669.2
GSM15966	1677.9	GSM15969	184
GSM15967	781.4	GSM15970	1006.2

Moreover, it is commonly known that slow wound healing is associated with the diabetic condition (see, e.g., Jerry Ryan, *The Lowdown on High Blood Sugar*, website <http://www.flickergaming.net/the-lowdown-on-high-blood-sugar-by-jerry-ryan--ph-d.html> (downloaded Jan. 31, 2008)). Applicants submit that the methods of the invention can be used to treat wounds in all such SLPI-deficient mammals.

The specification as filed fully enables treatment of wounds and inflammation in SLPI-deficient mammals with wounds by administration of PEPI. Thus, as explained above, the specification demonstrates that exogenous PEPI can restore normal wound healing in SLPI-null mice (see Example 6). The specification further describes how to make PEPI, for example, in the Examples, at page 9, line 1 to page 16, line 15, and at page 23, line 11 to page 30, line 29. In addition, the specification describes methods for administering PEPI in the Examples and at page 31, line 1 to page 39, line 4. Accordingly, the specification clearly enables one of skill in the art to make and use the invention.

Withdrawal of this rejection under 35 U.S.C. § 112, first paragraph, is respectfully requested.

#### ***§112, Second Paragraph, Rejection of the Claims***

Claims 17, 18, 40, 41, 59 and 61 were rejected under 35 U.S.C. § 112, second paragraph, as allegedly indefinite.

Applicant submits that indefiniteness depends on whether one of skill in the art would understand the scope of the claim when the claim is read in light of the specification. *North American Vaccine Inc. v. American Cyanamid Co.*, 7 F.3d 1571, 28 USPQ2d 1333 (Fed. Cir. 1993). If the claims read in light of the specification reasonably apprise those skilled in the art of the scope of the invention, § 112 demands no more. *Miles Laboratories Inc. v. Shandon, Inc.*, 997 F.2d 870, 27 USPQ2d 1123 (Fed. Cir. 1993).

The issues raised by the Examiner with respect to different claims are separately discussed below.

**Claims 4 and 27**

The Examiner alleges that the term “the” should be used instead of “an” in claims 4 and 27. The term “an” has been deleted from claims 4 and 27. Applicant submits that the language of claims 4 and 27 is clear and definite. Withdrawal of this rejection under 35 U.S.C. § 112, second paragraph, is respectfully requested.

**Claims 17 and 18**

The Examiner alleges that the term “claim” should be used instead of “claims” in claims 17 and 18. Applicant has made this amendment and submits that the language of claims 17 and 18 is clear and definite. Withdrawal of this rejection under 35 U.S.C. § 112, second paragraph, is respectfully requested.

**Claims 18 and 59**

The Examiner alleges that claims 18 and 59 should depend from claim 2. Applicant has made this amendment and submits that the language of claims 18 and 59 is clear and definite. Withdrawal of this rejection under 35 U.S.C. § 112, second paragraph, is respectfully requested.

**Claims 40 and 41**

The Examiner alleges that the term “claim” should be used instead of “claims” in claims 40 and 41. Applicant has made this amendment and submits that the language of claims 40 and 41 is clear and definite. Withdrawal of this rejection under 35 U.S.C. § 112, second paragraph, is respectfully requested.

**Claims 41 and 61**

The Examiner alleges that claims 41 and 61 should depend from claim 25. Applicant has made this amendment and submits that the language of claims 41 and 61 is clear and definite. Withdrawal of this rejection under 35 U.S.C. § 112, second paragraph, is respectfully requested.

**CONCLUSION**

Applicant respectfully submits that the claims are in condition for allowance, and notification to that effect is earnestly requested. The Examiner is invited to telephone Applicant's attorney at (516) 795-6820 to facilitate prosecution of this application.

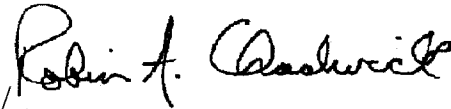
If necessary, please charge any additional fees or credit overpayment to Deposit Account No. 19-0743.

Respectfully submitted,

SCHWEGMAN, LUNDBERG & WOESSNER, P.A.  
P.O. Box 2938  
Minneapolis, MN 55402  
(516) 795-6820

Date February 1, 2008

By

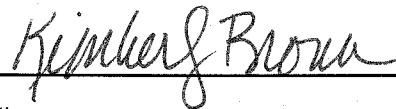


Robin A. Chadwick  
Reg. No. 36,477

**CERTIFICATE UNDER 37 CFR 1.8:** The undersigned hereby certifies that this correspondence is being filed using the USPTO's electronic filing system EFS-Web, and is addressed to: Mail Stop Amendment, Commissioner of Patents, P.O. Box 1450, Alexandria, VA 22313-1450 on this 1<sup>st</sup> day of February 2008.

KIMBERLY BROWN

Name



Signature